Plasma talin is a new diagnostic and monitoring marker for rheumatoid arthritis

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ABSTRACT

Background/Purpose: Anti-CCP antibody (ACPA) has been reported to as a useful and highly specificity marker for the diagnosis of rheumatoid arthritis (RA). However, more sensitive diagnostic biomarker might be expected because the sensitivity of ACPA in early RA has been shown to be lower than expected. Talin is a protein that completes the link between integrins and the actin cytoskeleton, and plays an important role in the establishment of focal adhesions. In this paper, we focused on plasma talin as a diagnostic marker for RA.
Method: RA was diagnosed as the 2010 Rheumatoid Arthritis Classification Criteria. Plasma and sera were obtained simultaneously from 50 RA patients (Age, 60.9±14.4 y/o; DAS28, 5.23 ± 1.11) and 70 controls (Ctrl) (30 osteoarthritis (OA) patients, 20 SLE patients, and 20 normal healthy controls (NC)). Twenty-two (44.0 %) of these 50 RA patients were early-onset (≤ 6 months) RA and 39 (78.0 %) of these patients were untreated at the time of collecting blood. Plasma talin was quantified using a sandwich ELISA with anti-talin capture and detecting antibodies. Serum ACPA was measured using a commercial ELISA kit. Plasma was obtained at baseline and 14 weeks after treatment with IFX from 5 RA patients who entered remission (SDAI<3.3) (Remission group) and 5 RA patients who did not enter remission (Non-remission group) at 14 weeks after IFX treatment.
Results: Plasma level of talin was significantly (p<0.0001) higher in RA patients (177.3 ± 167.3 ng/mL) than in OA (28.8 ± 29.7 ng/mL), SLE (38.1 ± 38.0 ng/mL), and NC (41.9 ± 51.3 ng/mL), respectively. The area under ROC curve (AUC) of talin (0.902) was larger than AUC of ACPA (0.770) in differentiation between RA and Ctrl. Moreover, the sensitivity of talin (82.3%) for the diagnosis of RA was higher than that of ACPA (58.0%), rheumatoid factor (Rf) (76.1%), and MMP-3 (74.0%) while its specificity (85.1%) was higher than that of Rf (57.0%) and MMP-3 (55.3%). Interestingly, the plasma level of talin before treatment (PRE) was significantly (p<0.001) down-regulated to the normal range (<50 ng/mL) after IFX treatment (POST) in Remission group whereas it did not reduce to the normal range in Non-remission group.
Conclusion: Our findings suggest clinical usefulness of plasma talin as a new diagnostic and monitoring biomarker for RA.

METHODS

1) Patients and controls

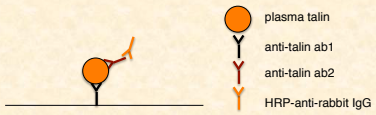
i) RA patients (n= 50): fulfilled 2010 ACR/EULAR Criteria

Age:	60.9 ± 14.4 y/o
Disease duration:	35.0 ± 56.4 months
Early onset (< 6mo):	44.0% (22/50)
DAS28:	5.23 ± 1.11
No treatment:	78.0% (39/50)

ii) Controls

a) Normal healthy controls	(n=30)
b) osteoarhritis (OA)	(n=20)
c) systemic lupus erythematosus(SLE)	(n=20)

2) Quantification of plasma talin
<sandwich ELISA>



Plasma talin was evaluated using a sandwich ELISA with anti-talin ab1 (H-18: goat polyclonal anti-talin antibody) and anti-talin ab2 (developed from rabbits immunized with talin F1 portion) and quantified using a talin synthesized polypeptide as a standard.

3) Quantification of serum ACPA

Serum ACPA (anti-CCP antibody) was quantified using a commercial ELISA kit (MESACUP CCP TEST)

RESULTS

Fig.1

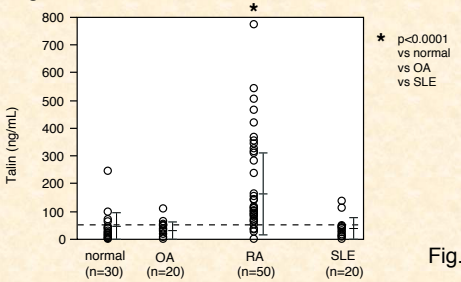


Fig.1 Plasma talin is up-regulated in RA patients.
Plasma talin was quantified using a sandwich ELISA. As a result, Plasma talin of RA patients (177.3 ± 167.3 ng/mL) was significantly (p<0.0001) up-regulated compared with those of normal healthy controls (41.9 ± 51.3), OA patients (28.8 ± 29.7), and SLE patients (38.1 ± 38.0).

Fig.2

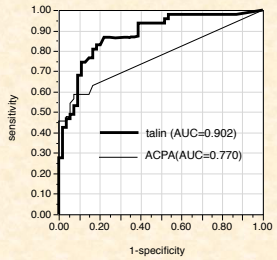


Fig.2 Diagnosis ability of plasma talin for RA.
The area under ROC curve (AUC) of talin (0.902) was larger than AUC of ACPA (0.770) in differentiation between RA (n=50) and Controls (n=70, normal healthy controls, OA, SLE). Cut-off value of plasma talin for the diagnosis of RA was 51.7 ng/mL from this ROC analysis.

Table 1. Sensitivity and specificity of plasma talin for the diagnosis of RA

	Sensitivity(%)	Specificity(%)
talin	82.0	85.0
ACPA	58.0	91.0
Rf	76.0	57.0
MMP-3	74.0	55.0

Sensitivity and specificity of plasma talin (> 51.7 ng/mL), serum ACPA (> 4.5 UmL), serum Rf (> 20 IU/mL), and serum MMP-3 (> 60 ng/mL) for the diagnosis of RA was estimated in 50 RA and 70 Controls.

Fig.3

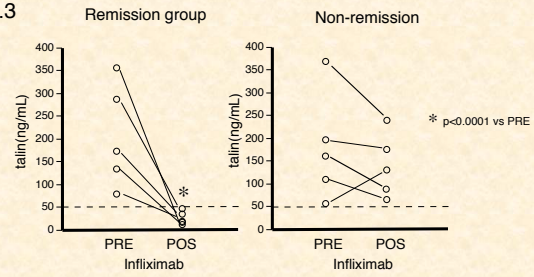


Fig 3. Plasma talin can be useful for monitoring the RA treatment. Plasma level of talin before treatment (PRE) was significantly (p<0.001) down-regulated to the normal range (<50 ng/mL) after infliximab treatment (POST) (14 weeks) in Remission group whereas it did not reduce to the normal range in Non-remission group.

CONCLUSION

Plasma talin could be a new diagnostic and monitoring biomarker for RA.